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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,523	08/17/2005	Barton Haynes	1579-968	7798

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
05/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,523	HAYNES ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 11 February 2008. Claims 1-20 are pending.

Election/Restriction

Applicant's election of Group I, claims 1-17, in the reply filed on 11 February 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 18-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-17 are currently examined.

Priority

Acknowledgement is hereby made of Applicant's claim for priority under 35 U.S.C. 371 to international application PCT/US03/22917, filed 23 July 2003, and under 35 U.S.C. 119(e) to United States Provisional Application No. 60/397,605 filed 23 July 2002. The presently claimed subject matter is fully supported by the disclosure of this U.S. Provisional Application, benefit to this earlier filed U.S. Provisional Application has been granted. The effective filing date of the instant application is 23 July 2002.

Information Disclosure Statement

Applicant's Information Disclosure Statements (IDS) filed 21 December 2004 (three pages total) has been received and entered into the application. As reflected by the attached, initialed and signed copy of form PTO-1449A, the Examiner has considered the cited references.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ross *et al.* (2001, hereinafter "Ross") in view of Shearer *et al.* (1995, hereinafter "Shearer"), as evidenced by Rizzuto *et al*. (1998).

The instant claims are directed to a fusion protein comprising: (i) an IgG Fc component, (ii) an HIV envelope (Env) component, and (iii) a C3d component; and a composition comprising the fusion protein.

Ross discloses a DNA vaccine expressing a fusion protein of murine C3d fused to the C-terminus of HIV Env gp120 (recited in claim 9) that is administered into mice with gold beads as a carrier (recited in claims 11 and 12). See pages 2-3. Ross further discloses that one consequence of complement activation is the covalent attachment of the C3d to antigen. C3d in turn binds to CD21 on B lymphocytes (recited in claim 8),

which ultimately amplifies B cell activation and antibody production. See page 2, middle full paragraph.

Ross does not specifically describe a fusion protein of HIV Env gp120 and human C3d. However, Ross discloses that in the human immune system, C3d is one of the final degradation products of the third complement protein, C3. See page 2, middle full paragraph. Thus, Ross provides the motivation to make a fusion protein of HIV Env gp120 and human C3d (recited in claim 7) when the host to be administered the immunogen is changed from mice to human. As evidenced by Rizzuto *et al*. (1998), the gp120 protein comprises the V3 domain towards its C-terminus and includes a B cell neutralizing antibody epitope.

Ross does not disclose the IgG Fc component of the claimed fusion protein.

Shearer discloses a fusion protein by fusing the gp120 binding domain of CD4 to the Fc portion of the human IgG1 (recited in claim 6) heavy chain. See Abstract and page 281. This chimeric protein retains certain properties of human IgG, including a prolonged half-life in serum and Fc receptor binding. See page 281, the sentence connecting the left and right column. Furthermore, Shearer discloses linkers composed of two repeats of four glycines and a serine were fused at the junctions of Env and C3d (recited in claim 5). See page 3, lines 7-8.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the human IgG Fc component to either the N-terminus (recited in claims 1-4) or the C-terminus of Ross' fusion protein of gp120-C3d for the purpose of increasing the serum half-life of gp120-C3d. The skilled artisan would have

a reasonable expectation of success because Shearer suggests that human IgG Fc prolongs the serum half-life of the gp120 binding domain of CD4. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 13, 14, 16 and 17 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ross *et al.* (2001, hereinafter "Ross") in view of Shearer *et al.* (1995, hereinafter "Shearer") and DeVico *et al*. (US 5,518,723, hereinafter "DeVico"), as evidence by Rizzuto *et al*. (1998).

The instant claims are directed to a complex comprising a fusion protein comprising: (i) an IgG Fc component, (ii) an activated ligand-bound HIV envelope (Env) component, and (iii) a C3d component

The disclosure of Ross and Shearer is set forth above. Neither reference discloses a ligand-bound HIV Env.

DeVico teaches an immunogen, called gp120-CD4 complex, which is the recombinant HIV envelope protein gpl20 chemically crosslinked to a soluble CD4 ligand (column 1, lines 7-12). DeVico further teaches that the gp120-CD4 immunogen exposes cryptic epitopes on gp120 that induces neutralizing antibodies to gp120 (column 7, lines 37-47). Still further, DeVico teaches that the CD4-complexed gp120 appears to undergo a conformational change that present an array of epitopes (recited in claim 13) that were hidden on the uncomplexed glycoprotein. Covalently bonded CD4-gp120 complexes are useful for raising neutralizing antibodies against various

isolates of HIV-1 and against HIV-2 (column 1, lines 57-67; column 2, lines 1-2). As evidenced by Rizzuto *et al*., CD4 binding to HIV gp120 can induce (up-regulate) the CCR5 binding site on gp120, facilitating HIV fusion to a host cell via CCR5 co-receptor (whole document, particularly Abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the human IgG Fc component to either the N-terminus (recited in claims 1-4) or the C-terminus of Ross' fusion protein of gp120-C3d for the purpose of increasing the serum half-life of gp120-C3d, and to further modify the fusion protein by crosslinking a CD4 molecule to the middle component, HIV Env gp120, so as to raise neutralizing antibodies. The skilled artisan would have a reasonable expectation of success because Shearer suggests that human IgG Fc prolongs the serum half-life of the protein that the IgG Fc is fused to and because DeVico teaches that CD4-complexed gp120 raises non-strain-specific neutralizing antibodies against both HIV-1 and HIV-2. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 13-15 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ross *et al.* (2001, hereinafter "Ross") in view of Shearer *et al.* (1995, hereinafter "Shearer") and Wyatt (1995, hereinafter "Wyatt").

The instant claims are directed to a complex comprising a fusion protein comprising: (i) an IgG Fc component, (ii) an HIV envelope (Env) component bound to an antibody, and (iii) a C3d component.

The disclosure of Ross and Shearer is set forth above. Neither reference discloses a ligand-bound HIV Env.

Wyatt discloses a complex comprising HIV gp120 bound to a monoclonal antibody (recited in claim 15), which is shown as the wild-type gp120-17b and wild-type gp120-48d control in precipitation in Figure 2A and B (see also page 5726, right column, last paragraph) and as the wild-type gp120-A32 control in Figure 4 and Figure 5 (see also page 5728, right column). Upon the binding of soluble CD4, HIV gp120 experiences conformational changes and up-regulates (exposes) the conserved, discontinuous epitope on the HIV gp120. The binding of the A32 antibody to the wild type envelope glycoprotein gp120 activates the gp120 so that mAbs 17b and 48d recognize and bind to the exposed conformational epitopes and form gp120/mAb A32/17b or gp120/mAb A32/48d complex. See page 5728, right column and Figure 5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the human IgG Fc component to either the N-terminus (recited in claims 1-4) or the C-terminus of Ross' fusion protein of gp120-C3d for the purpose of increasing the serum half-life of gp120-C3d, and to further modify the fusion protein by binding an antibody to the middle component, HIV Env gp120, so as to raise more neutralizing antibodies. The skilled artisan would have a reasonable expectation of success because Shearer suggests that human IgG Fc prolongs the serum half-life of the protein that the IgG Fc is fused to and because Wyatt teaches that mAb-complexed gp120 exposes more epitopes for other neutralizing antibodies. Thus, the invention as

a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the application as filed so as not to add new matter. See MPEP §714.02 and §2163.06.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648